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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,230	06/14/2007	Chikara Murakata	P28933	4996

7055 7590 03/05/2009

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EXAMINER	
YOUNG, SHAWQUIA	

ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
03/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/560,230	MURAKATA ET AL.	
	Examiner	Art Unit	
	SHAWQUIA YOUNG	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *31-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/1/06, 4/10/07, 5/10/07, 8/5/08 and 11/17/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-34 are currently pending in the instant application.

I. *Priority*

The instant application is a 371 of PCT/JP04/08375, filed on June 9, 2004 and claims benefit of Foreign Applications JAPAN 2003-164727, filed on June 10, 2003 and JAPAN 2004-121324, filed on April 16, 2004.

II. *Information Disclosure Statement*

The information disclosure statements (IDS) submitted on December 1, 2006, April 10, 2007, May 10, 2007, August 5, 2008 and November 17, 2008 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

III. *Restriction/Election*

A. Election: Applicant's Response

Applicants' election with traverse of Group I in the reply filed on December 17, 2008 is acknowledged. The traversal is on the ground(s) that: (1) the Examiner has not established that the claims lack unity of invention under PCT Rule 13.1 and 37 CFR 1.475.

All of the Applicants' arguments have been considered but have not been found persuasive. It is pointed out that the restriction requirement is made under 35 U.S.C. 121. 35 U.S.C. 121 gives the Commissioner (Director) the authority to restrict

applications to several claimed inventions when those inventions are found to be independent and distinct. The Examiner has indicated that more than one independent and distinct invention is claimed in this application and has restricted the claimed subject matter accordingly.

Applicants argue that the Examiner has not established that the claims lack unity of invention under PCT Rule 13.1 and 37 CFR 1.475. However, the Examiner wants to point out that it clearly states under rule 13.2, "Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art." Since Applicants wanted to emphasize rule 37 CFR 1.475, the Examiner wants to emphasize that rule 13.2 is also disclosed in part (a) of 37 CFR 1.475. So according to 37 CFR 1.475 (a), Applicants' claims contain a special technical feature(s) which have to make a contribution over the prior art. Applicants' special technical feature which is based on the structure of formula I does not make a contribution over the prior art (See, RN 462106-02-1) and therefore lack unity of invention. **The restriction is deemed proper and made final.** The Examiner wants to make clear that once the elected product claims are deemed allowable then the process claims relating to the elected product claims will be rejoined (See MPEP 821.04).

The Examiner wants to further point out that different search considerations are involved (i.e., class/subclass searches, databases searches, etc.) for each of the groups listed. The inventions are classified into classes 514, 544, 546 and 548. However, each Class 514, 544, 546 and 548 encompasses numerous patents and published applications. For instance, Class 514 contained 165,171 patents and published applications. Therefore it would constitute a burden on the Examiner and the Patent Office's resources to examine the instant application in its entirety.

Subject matter not encompassed by elected Group I are withdrawn from further consideration pursuant to 37 CFR 1.142 (b), as being drawn to nonelected inventions.

IV. Rejections

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, there are brackets, parenthesis, etc. present in the definitions of the variables found in formula (I) in claims 1-30. It is unclear what subject matter is actually being claimed with the numerous brackets, parenthesis, etc. being used in the instant claims.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue".

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and

8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention is drawn to an antitumor agent which comprises the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 1 as an active ingredient.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is the more specific enablement is necessary in order to satisfy the statute. Applicants' claims are drawn to pharmaceutical agents for the treatment of diseases. According to Applicants' specification on page 120, the claimed compounds can be used to treat a malignant tumor (breast cancer, gastric cancer, ovarian cancer, colon cancer, etc.).

The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanisms, and consequently, differ in treatment protocol. Cancer is a disease characterized by a population of cells that grow and divide without respect to normal limits, invade and destroy adjacent tissues, and may spread to distant anatomic sites through a process called metastasis (URL:http://en.wikipedia.org/wiki/ Cancer>). Most cancers are named for where they start. For example, lung cancer starts in the lung, and breast cancer starts in the breast. Symptoms and treatment depend on the cancer type and how advanced it is (URL: <http://www.nlm.nih.gov/medlineplus/cancer.html>>). It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531). Treatment may include surgery, radiation, chemotherapy, immunotherapy, monoclonal antibody therapy, etc. Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them. It is also known in the prior art (Lala et al. page 91) that the role of NO in tumor biology remains incompletely understood with both the promotion and inhibition of NO mentioned for the treatment of tumor progression and only certain human cancers may be treated by selected NO-blocking drugs. These example shows that there are different cellular mechanisms, the unpredictability in the

art and the different treatment protocols. Because "cancer" refers to a class of diseases, it is unlikely that there will ever be a single "cure or treatment for cancer".

The amount of direction present and the presence or absence of working examples

The only direction or guidance present in the instant specification is minimal. There are no working examples present for the treatment of any type of malignant tumor.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims

The breadth of the claims is drawn to an antitumor agent which comprises the thiadiazoline derivative or a pharmacologically acceptable salt thereof according to claim 1 as an active ingredient.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in

the art would need to determine what diseases out of all conditions would be benefited by the activity of the claimed compounds and would furthermore then have to determine which of the claimed compounds in the instant invention would provide treatment of the diseases.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* or *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

The specification fails to provide sufficient support of the broad use of the claimed compounds as an antitumor agent. As a result necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of the invention in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the

compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome, for example, by deleting claim 30.

V. *Objections*

Claim Objection-Non Elected Subject Matter

Claims 1-30 are objected to as containing non-elected subject matter. To overcome this objection, Applicant should submit an amendment deleting the non-elected subject matter.

VI. *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 7:00 AM-3:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shawquia Young/
Examiner, Art Unit 1626

/Rebecca L Anderson/

Primary Examiner, Art Unit 1626